Attorney Docket No.: PENN-0789
Inventors: Siegel et al.
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REMARKS

Claims 1-10 are pending in the instant application. Claim 1-10 have been rejected. Claims 1 and 4 have been amended, as supported throughout the specification and in particular at page 4, lines 21-24, page 8, lines 16-20 and page 13, lines 11-20. No new matter is added by this amendment. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Objection to Disclosure

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser executable code. Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended the specification to inactivate the link. No new matter is added by this amendment and entry is respectfully requested. Withdrawal of this objection in light of the amendments to the specification is respectfully requested.

II. Rejection of Claim 4 under 35 U.S.C. 112, first paragraph

The Examiner has maintained the rejection of claim 4 under 35 U.S.C. § 112 first paragraph. The Examiner suggests that the specification while being enabling for acetone does not reasonably provide enablement for all organic solvents. The Examiner suggests that acetone is the only organic solvent that is disclosed in the specification

and that it would require a skilled artisan an unreasonable amount of experimentation to ascertain those solvents which are suitable for the haloperidol-lactide-glycolide system.

Applicants respectfully disagree as it is well within the routine skill of those in this art field to substitute other organic solvents for acetone as exemplified in the instant specification.

However, in an earnest effort to advance the prosecution of this case, Applicants have amended claim 4 to specify acetone.

Withdrawal of this rejection is therefore respectfully requested.

III. Rejection of Claim 1 and 2 under 35 U.S.C. § 102(b)

The Examiner has maintained the rejection of claims 1 and 2 under 35 U.S.C. § 102(b) as being anticipated by Kino et al. (WO 94/10982). As this reference is in Japanese, Applicants have reviewed in detail the teachings of U.S. Patent 5,871,778 which claims priority to this PCT application. The Examiner suggests that there is a recognition in Kino that the haloperidol-biodegradable polymer device is implantable. Further, the Examiner suggests that the ability to remove the drug delivery system has no patentable weight in the instant claims.

Applicants respectfully traverse this rejection.

The depot formulation taught by Kino et al. is very different from the instant claimed invention. For example, as taught at col. 3, lines 49 through 57 of U.S. Patent 5,871,778, the microsphere preparation of Kino is prepared by dissolving or dispersing a hydrophobic antipsychotic drug in a solution prepared by dissolving an in vivo histocompatible high molecular weight polymer in a solvent to give an oil layer. This oil layer is added to a water layer and subjected to an emulsification treatment. Thereafter, the microsphere preparation is obtained by removing the solvent in the oil layer by means of an in-water drying method. Thus, neither solvent casting nor compression molding, as required in the instant claimed invention, are taught by Kino et al. to fabricate their microspheres.

Further, Kino teaches at col. 7, lines 40-43, that the desired pharmacological effects upon injection of their microspheres can be obtained continuously by one injection per 1 to 8 weeks. In contrast, as taught at page 13, lines 11-20, of the instant application, the implants of the present invention deliver steady state concentrations of haloperidol for five months or more.

In an earnest effort to further distinguish the present invention from microsphere depot formulations such as taught by Kino et al. Applicants have amended the claims in

accordance with teachings at page 13, lines 11-20 to state that the surgically implantable drug delivery system is for delivery of steady state concentrations of haloperidol to a patient for 5 months or more.

Further, Applicants respectfully disagree with the Examiner that the characteristic of removability of the implant has no patentable weight. Removability of the implant is a structural characteristic of the implant resulting from its design and production process wherein solvent casting and compression molding are used to produce a single implantable device. This structural characteristic distinguishes the implantable device of the present invention from prior art teachings such as Kino et al. relating to administration of multiple microspheres, which quite clearly are not designed to be removed once administered.

In an earnest effort to answer the Examiner's query regarding when the system is removable and removable from what or where, Applicants have amended the claims in accordance with teachings at page 4, lines 21-24 and page 13, lines 11-20 to state that the implant is removable from a patient into which the drug delivery system has been implanted in the event the patient exhibits unwanted side effects following implantation. The Examiner seems concerned that bioerodibility may affect removability of the

implant. However, as discussed in the preceding paragraph and made clear in the claims as amended, these implants are designed and produced by a method which provides for long term, meaning five months or more, delivery of haloperidol. Thus, there is clearly a sufficient period of time for removal of the implant should unwanted side effects be observed.

Since Kino et al. does not teach the elements of solvent casting and compression molding, an implantable delivery system which delivers steady state concentrations of haloperidol to a patient for 5 months or more, and removability, this reference cannot anticipate the instant claimed invention. See MPEP § 2131.

Withdrawal of this rejection under 35 U.S.C. 102(b) is therefore respectfully requested.

IV. Rejection of Claims 1-3 under 35 U.S.C. § 102(b)

The Examiner has maintained the rejection of claims 1-3 under 35 U.S.C. § 102(b) as being anticipated by Cheng et al. In response to Applicants' amendment submitted June 10, 2004, the Examiner suggests that the characteristic of removability has no patentable weight.

Applicants respectfully traverse this rejection.

At the outset, Applicants respectfully disagree with the Examiner that the characteristic of removability of the implant has no patentable weight. As discussed in Section

III, supra, removability of the implant is a structural characteristic of the implant resulting from its design and a production process wherein solvent casting and compression molding are used to produce a single implantable device. This structural characteristic distinguishes the implantable device of the present invention from prior art teachings such as Cheng et al. relating to administration of multiple microspheres, which quite clearly are not designed to be removed once administered.

Further, beginning at page 204, Cheng et al. teach a method for preparation of a depot formulation of haloperidol-loaded PLG microspheres which involves emulsification-solvent evaporation, not solvent casting and compression molding as set forth in the instant claimed invention. Cheng et al. also teach at page 203 that their depot formulations have the advantage in that a patient can receive an intramuscular injection every three to four weeks. In contrast, the solvent casted and compression molded implants of the present invention are designed to deliver steady state concentrations of haloperidol for five months or more. The claims have been amended in accordance with teachings at page 13, lines 11-20 to include this distinguishing element.

Thus, since Cheng et al. does not teach the elements of solvent casting and compression molding, an implantable

delivery system which delivers steady state concentrations of haloperidol to a patient for 5 months or more, nor removability, this reference cannot anticipate the instant claimed invention. See MPEP § 2131.

Withdrawal of this rejection under 35 U.S.C. § 102(b) is therefore respectfully requested.

V. Rejection of Claims 1-6 under 35 U.S.C. 102(e)

Claims 1-6 have been rejected under 35 U.S.C. 102(e) as being anticipated by Brodbeck et al. The Examiner suggest that Brodbeck discloses methods and compositions for systemically or locally administering by implantation a beneficial agent to a subject and that haloperidol is listed as a beneficial agent. Further, the Examiner suggests that the composition of Brodbeck comprises 50:50 poly(lactide-co-glycolide) copolymers and that in the preparation solvents are involved. The Examiner also suggests that the implant of Brodbeck has the option of being removable.

Applicants respectfully traverse this rejection.

Teachings of Brodbeck relate to a gel composition comprising both a polymer and a biocompatible solvent. A method for production of these gels is set forth beginning at col. 17, line 51. It is taught therein that the viscous gel is formed by mixing the polymer and the solvent and that mixing can be achieved with conventional low shear equipment such as a Ross double planetary mixer. No where does

Brodbeck et al. teach solvent casting or compression molding to produce an implantable drug delivery device as claimed.

Further, at col. 22, lines 6-10 Brodbeck teaches that release rates on the order of from about 0.1 to 100 micrograms/day for periods of about 7 to about 90 days can be obtained.

In contrast, the implants of the present invention produced by solvent casting and compression molding deliver steady state concentrations of haloperidol for 5 months or more. As discussed in Sections III and IV, the claims have been amended to include this limitation in accordance with teachings at page 13 of the instant specification.

Since Brodbeck teaches neither an implant produced by solvent casting and compression molding nor a device which delivers steady state concentrations for 5 months or more, this reference cannot anticipate the instant claimed invention. See MPEP 2131.

Withdrawal of this rejection under 35 U.S.C. § 102(e) is therefore respectfully requested.

VI. Rejection of Claims 4-10 under 35 U.S.C. § 103

Claims 4-10 have been rejected under 35 U.S.C. § 103 as being unpatentable over Cheng et al. The Examiner suggests that the difference between Cheng and the instant claims is that Cheng does not specifically state that the composition is formulated as an implant. However, the Examiner suggests

that it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare haloperidol-poly(lactide-co-glycolide)copolymer compositions. The Examiner suggests that one having ordinary skill in the art would have been motivated to formulate the composition into an implant with the expectation of improving degree of compliance and more predictable absorption.

Applicants respectfully traverse this rejection.

While Applicants agree with the Examiner that Cheng is different from the instant invention in that the composition is not taught to be formulated as an implant, there are multiple additional differences between the teachings of Cheng et al. and the instant claimed invention.

For example, no where does Cheng teach a step of solvent casting the haloperidol and biodegradable polymer solution to produce a completely dry haloperidol-polymer material as set forth in step b) of claim 4 or molding under compression the dry haloperidol-polymer material into a surgical implant as set forth in step c) of claim 4. Further, no where is it taught or suggested that the depot formulations of Cheng are removable. In addition, Cheng et al. teach at page 203 that their depot formulations have the advantage in that a patient can receive an intramuscular injection every three to four weeks. In contrast, the

claims have been amended in accordance with teachings at page 13 to state that the delivery system delivers a steady state concentration of haloperidol for 5 months or more.

Thus Cheng et al. neither teaches or suggests a device with all the limitations of the instant claimed invention nor provides any reasonable expectation of success that an implant prepared by solvent casting and compression molding in accordance with the instant claimed invention would successfully deliver steady state concentrations of haloperidol. Thus, this reference cannot establish a prima facie case of obviousness. See MPEP 2143.

Withdrawal of this rejection under 35 U.S.C. § 103 is therefore respectfully requested.

VII. Rejection of Claims 7-10 under 35 U.S.C. § 103

Claims 7-10 have been rejected under 35 U.S.C. § 103 as being unpatentable over Brodbeck et al. (U.S. Patent 6,130,200). The Examiner has acknowledged that Brodbeck does not disclose treating psychotic conditions. However, the Examiner suggests that it is known that haloperidol is an antipsychotic agent it would have been obvious to one of ordinary skill in the art at the time the invention was made to implant the haloperidol composition in a subject in need of treatment.

Applicants respectfully traverse this rejection.

Claims 7-10 are dependent claims which depend from claim 1. Thus, in accordance with MPEP § 2143.03 for claims 7-10 to be obvious in light of Brodbeck, claim 1 must also be obvious in light of Brodbeck.

However, as already discussed in detail in Section V, supra, Brodbeck does not teach an implant produced by solvent casting and compression molding. Brodbeck also does not teach a device which delivers steady state concentrations for 5 months or more. Nor is there any suggestion in Brodbeck of a drug delivery device with these characteristics.

Accordingly, the teachings of Brodbeck fail to provide the requisite teaching or suggestion of all the claim limitations to render the instant invention obvious. Further, the teachings of Brodbeck fail to provide any reasonable expectation of success with respect to the instant claimed invention. Thus, this reference cannot establish a prima facie case of obviousness with respect to claim 7-10 or claim 1. See MPEP § 2143.

Withdrawal of this rejection under 35 U.S.C. 103 is therefore respectfully requested.

VIII. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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